US Army Medical Research and Materiel

Technology Available for Licensing

Method of Treating, Preventing or Inhibiting Central Nervous System Injuries and Diseases

Features and advantages:

- **ALA already proven as safe clinical treatment for peripheral neuropathy in humans**
- **Combined ALA and DHLA pretreatment of rats reduces seizures by 55% in an epilepsy model**
- **DHLA protects against spinal cord injury in rats, *in vivo***
- **DHLA protects against hemoglobin-induced toxicity in cultured rat neurons, *in vitro***

This invention provides a method of treating, preventing, or inhibiting a central nervous system (CNS) injury or disease, neurotoxicity or memory deficit by the administration of at least one lipoic acid compound to the subject. Conditions likely to cause CNS injury include traumatic brain injury, post-traumatic epilepsy, stroke, cerebral ischemia, neurodegenerative diseases, blunt objects impacting the head, and nerve agents. The lipoic compound may be alpha-lipoic acid (ALA), dihyrolipoic acid (DHLA or DHL), 2-(N,N-dimethylamine) ethylamido lipoate-HCL (LA-plus), the oxidized or reduced R- or S-isomers, a metabolite of ALA, or an analog thereof. ALA is a physiological constituent of mitochondrial membranes and an essential cofactor in the oxidative decarboxylation of alpha-keto acids such as pyruvate and alpha-ketoglutarate.

ALA is clinically safe for treating peripheral neuropathy in diabetic patients. It is stable in tablet form, is well tolerated when given orally, has good bioavailability in humans, and is endogenously converted to DHLA. Both ALA and DHLA were shown as neuroprotective in several rodent models of cerebral ischemia and were effective scavengers of reactive oxygen species (ROS). Formation of neurotoxic ROS appears to be part of the pathway that results in necrotic neuronal death.

Patent Status

nation of DHL and N-*tert*-Butyl-alpha-(2-sulfophenyl)nitrone (SPBN) or alpha-Phenyl-N-*tert*-butylnitrone (PBN) provided almost complete protection (86% and 82%, respectively) against H_2O_2-induced oxidative insult of cultured neurons. The compounds of [illegible]nvention could potentially be more effective in [illegible]tion with other ROS scavengers including coenzyme Q, vitamin E, vitamin C, pyruvate, melatonin, niacinamide, and N-acetylcysteine.

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KEYWORDS: alpha-lipoic acid; dihydrolipoic acid; nitrones; free radicals; free radical scavengers; brain injury; spinal cord injury; neurotoxicity; neuroprotection

Licensing Opportunities • Patent licenses are available to companies with commercial interests